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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/974,703 | 10/10/2001 | Douglas E. Vaughan | 1242/39/2 | 7969 |

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| EXAMINER | |
|---|---|
| LEITH, PATRICIA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1654 | |

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/974,703 | VAUGHAN, DOUGLAS E. | |
| | Examiner | Art Unit | |
| | Patricia Leith | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *38 and 40-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 40-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



RP

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/28/05 has been entered.

Claims 38 and 40-45 are pending in the application and were examined on their merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office Action.

### *Claim Rejections - 35 USC § 103*

Claim 38 remains rejected and claims 40-45 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (12/1998) in view of Vaughan (1997).

Applicant's arguments were fully taken into consideration, but were not convincing for the following reasons.

Applicant argues that the references do not teach every element of the claimed invention (regarding claim 38, p. 6- Arguments) since neither of the prior art documents teaches reducing a risk of cardiovascular disease in a post-menopausal female human subject (pp. 7-8 arguments). Further, Applicant alleges that ACE inhibition is ambiguous in light of the teaching by Lottermoser et al. and that "based on the teachings of Lottermoser et al., a skilled artisan in the field could infer that ACE inhibition has no effect in reducing PAI-1 in healthy subjects" (p. 7, Arguments). It is noted that the entire Lottermoser et al. reference has not been submitted to the Office and the Examiner will only discuss the matter disclosed in the Abstract as Applicant's reference 22 in the IDS dated 7/19/2002. Although Applicant argues that ACE inhibition is ambiguous, such as administration of captopril as indicated by Lottermoser et al. the claims do not refer to any particular ACE inhibitor, and can be drawn to any ACE inhibitor as taught by Brown et al.

Applicant further argues that "potential prophylactic uses for ACE inhibitors remained inconclusive" (p. 8, Arguments). However, again, the claims are drawn to any ACE inhibitor. It is also further noted that ACE inhibitors, as clearly shown in the prior art, were well known to be administered for preventing atherosclerosis events caused by activation of RAS (see first full paragraph p. 965, Brown et al.). One of ordinary skill

in the art would have had a reasonable expectation that administration of an ACE inhibitor to any person with an increased renin-sodium profile (as explained by Brown et al.) would have at least somewhat prevented cardiac risk. The ordinary artisan would have recognized that again, any person, healthy, or non-healthy, young or old, male or female, pre-menopausal, menopausal or post-menopausal who fell within this increased renin-sodium profile would have benefited from taking an ACE inhibitor in order to prevent or at least partially prevent a cardiac episode. Although Applicant stresses that the prior art did not specifically teach where an ACE inhibitor was administered to a post-menopausal woman, it is noted that the prior art need not teach every element of the claimed invention in order to render the claims obvious in light of the prior art. In the Instant case, because ACE inhibitors were already known to be effective, the ordinary artisan, again, would have had a reasonable to good expectation that ACE inhibitors would be effective in post-menopausal women.

Applicant argues that the Instant specification teaches that "subjects treated with the ACE inhibitor exhibited a statistically significant 38% decrease in plasma PAI-1" (p. 9, Arguments). However, this data is considered statistically significant with regard to the control. ACE inhibitors were already known in the art to decrease plasma PAI-1 and therefore this data is not deemed significant with regard to ACE inhibitors which were already known in the art to decrease plasma PAI-1. Applicant further argues that the Instant specification displays a synergistic effect with regard to combination therapy with ACE inhibitor and estrogen. It is noted that the features upon which applicant relies (i.e.,

combination therapy) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that "The study set forth.....unexpectedly provides protection against cardiovascular disease by lowering PAI-1 levels in the blood of subjects" (p. 9, Arguments). However, to reiterate, the ordinary artisan would have a reasonable to good expectation that the administration of an ACE inhibitor to any person, such as a post-menopausal woman would have decreased the likelihood of a cardiac situation (i.e., myocardial infarction) in view of the cited prior art references. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be *expressly suggested* in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981) (emphasis added).

## ***Conclusion***

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed

invention. Because the prior art teaches that ACE inhibitors reduce the production of endogenously produced PAI-1 which in turn prevents cardiac situations such as atherosclerosis. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No Claims are allowed.

This is an RCE of applicant's earlier Application No. 09/974,703. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia Leith
Primary Examiner
Art Unit 1654

6/7/05